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- <120> Diagnostic Use of Polymorphisms in the Gene Coding for the TNF Receptor II and Method for Detecting Non-Responders to Anti-TNF-Therapy

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| | | | cag Gln | | | | | | | | | | | | | 1313 |
| gat Asp | tcc Ser | agc Ser | ccc Pro 390 | Ser | gag Glu | tcc Ser | ccg Pro | aag Lys 395 | Asp | gag Glu | cag Gln | gtc Val | Pro | Phe | tcc Ser | 1361 |
| | | | Cys | | | | | Gln | | | | | Glu | | ctg Leu | 1409 |

ctg ggg agc acc gaa gag aag ccc ctg ccc ctt gga gtg cct gat gct 145° Leu Gly Ser Thr Glu Glu Lys Pro Leu Pro Leu Gly Val Pro Asp Ala 420 425 430

1505

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Ala Pro Glu Pro Gly Ser Thr Cys Arg Leu Arg Glu Tyr Tyr Asp Gln

35 40 45

Thr Ala Gln Met Cys Cys Ser Lys Cys Ser Pro Gly Gln His Ala Lys 55 Val Phe Cys Thr Lys Thr Ser Asp Thr Val Cys Asp Ser Cys Glu Asp Ser Thr Tyr Thr Gln Leu Trp Asn Trp Val Pro Glu Cys Leu Ser Cys 85 90 Gly Ser Arg Cys Ser Ser Asp Gln Val Glu Thr Gln Ala Cys Thr Arg 100 105 Glu Gln Asn Arg Ile Cys Thr Cys Arg Pro Gly Trp Tyr Cys Ala Leu 120 Ser Lys Gln Glu Gly Cys Arg Leu Cys Ala Pro Leu Arg Lys Cys Arg 135 Pro Gly Phe Gly Val Ala Arg Pro Gly Thr Glu Thr Ser Asp Val Val 150 155 Cys Lys Pro Cys Ala Pro Gly Thr Phe Ser Asn Thr Thr Ser Ser Thr 165 170 Asp Ile Cys Arg Pro His Gln Ile Cys Asn Val Val Ala Ile Pro Gly 185 Asn Ala Ser Met Asp Ala Val Cys Thr Ser Thr Ser Pro Thr Arg Ser 195 200 205 Met Ala Pro Gly Ala Val His Leu Pro Gln Pro Val Ser Thr Arg Ser 215 220 Gln His Thr Gln Pro Thr Pro Glu Pro Ser Thr Ala Pro Ser Thr Ser 230 235 Phe Leu Leu Pro Met Gly Pro Ser Pro Pro Ala Glu Gly Ser Thr Gly 245 250 Asp Phe Ala Leu Pro Val Gly Leu Ile Val Gly Val Thr Ala Leu Gly 265 Leu Leu Ile Ile Gly Val Val Asn Cys Val Ile Met Thr Gln Val Lys 280 Lys Lys Pro Leu Cys Leu Gln Arg Glu Ala Lys Val Pro His Leu Pro 295 Ala Asp Lys Ala Arg Gly Thr Gln Gly Pro Glu Gln Gln His Leu Leu 310 315 Ile Thr Ala Pro Ser Ser Ser Ser Ser Leu Glu Ser Ser Ala Ser 330 Ala Leu Asp Arg Arg Ala Pro Thr Arg Asn Gln Pro Gln Ala Pro Gly 340 345 Val Glu Ala Ser Gly Ala Gly Glu Ala Arg Ala Ser Thr Gly Ser Ser 360 Asp Ser Ser Pro Gly Gly His Gly Thr Gln Val Asn Val Thr Cys Ile 370 375 Val Asn Val Cys Ser Ser Ser Asp His Ser Ser Gln Cys Ser Ser Gln 385 390 395 Ala Ser Ser Thr Met Gly Asp Thr Asp Ser Ser Pro Ser Glu Ser Pro 405 410 Lys Asp Glu Gln Val Pro Phe Ser Lys Glu Glu Cys Ala Phe Arg Ser 420 425

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Leu Pro Leu Gly Val Pro Asp Ala Gly Met Lys Pro Ser
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Met Ala Pro Val Ala Val Trp Ala

-20 -15

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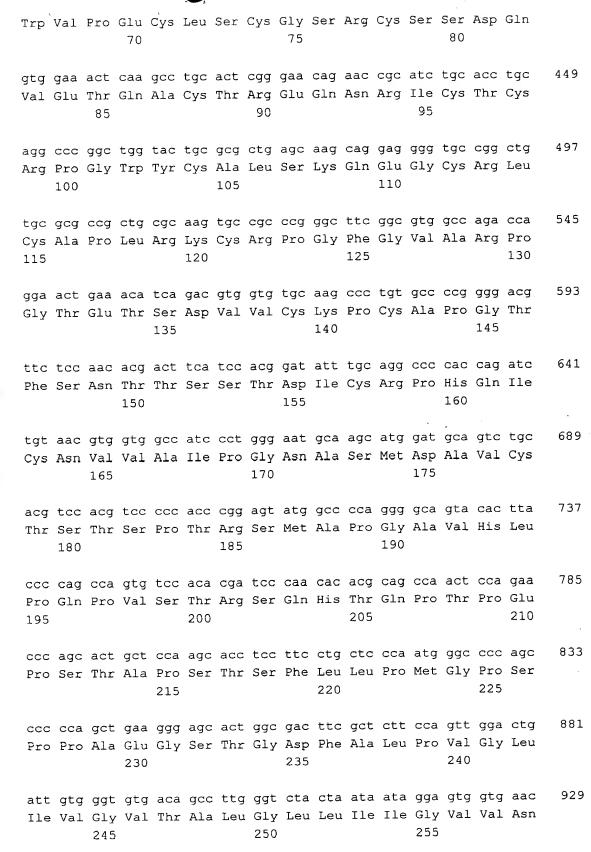
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Arg Leu Arg Glu Tyr Tyr Asp Gln Thr Ala Gln Met Cys Cys Ser Lys
20 25 30

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acc gtg tgt gac tcc tgt gag gac agc aca tac acc cag ctc tgg aac 353
Thr Val Cys Asp Ser Cys Glu Asp Ser Thr Tyr Thr Gln Leu Trp Asn
55 60 65

tgg gtt ccc gag tgc ttg agc tgt ggc tcc cgc tgt agc tct gac cag 401



tgt gtc atc atg acc cag gtg aaa aag aag ccc ttg tgc ctg cag aga

| | | | | | , | | | | | | | | _, | | | |
|------|------------|-----|------------|-----|------------|-------------------|------|-------|------|-------|------------|-------|-------|-----------------------|------------|------|
| 'Cys | Val 260 | Ile | Met | Thr | Gln | Val 265 | Lys | Lys | Lys | Pro | Leu 270 | Cys | Leu | Gln | Arg | |
| - | _ | - | | | | ttg Leu | | | | | | | | | | 1025 |
| | | | | | | ctg Leu | | | | | | | | | | 1073 |
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| | | | | | | tgc Cys | | | | | | | | | | 1265 |
| | | | | | | tcc Ser | | | | | | | | | | 1313 |
| | | | | | | tcc Ser | | | | | | | _ | | _ | 1361 |
| - | | | | | | cgg Arg | | | | | | | | | ctg Leu | 1409 |
| _ | | - | | _ | | aag Lys 425 | | _ | | | | | | | | 1457 |
| | | | ccc Pro | | taa 440 | ccaç | ggee | ggt (| gtgg | gctgi | tg to | cgta | gccaa | a | | 1505 |
| | | | , | | | . 4 | | | | ~~~ | a+ = | ~+ ~~ | | a a a a | | 1565 |

ggtgggctga gccctggcag gatgaccctg cgaaggggcc ctggtccttc caggccccca 1565

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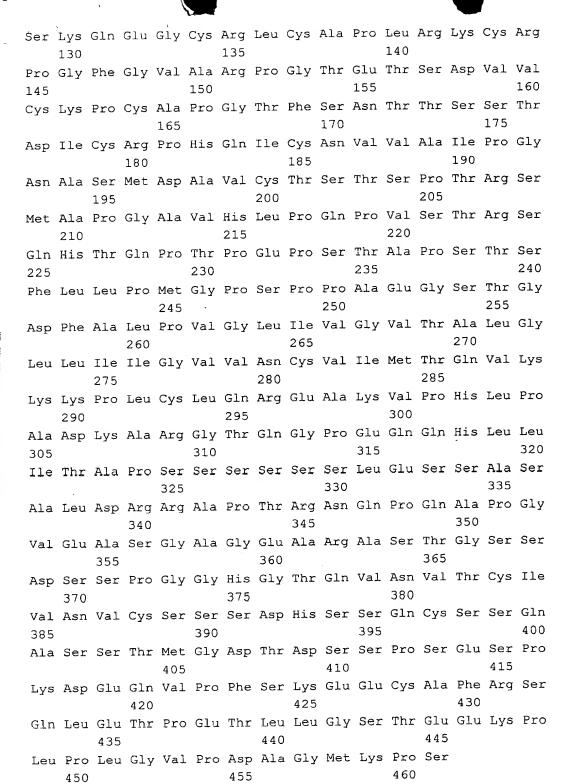
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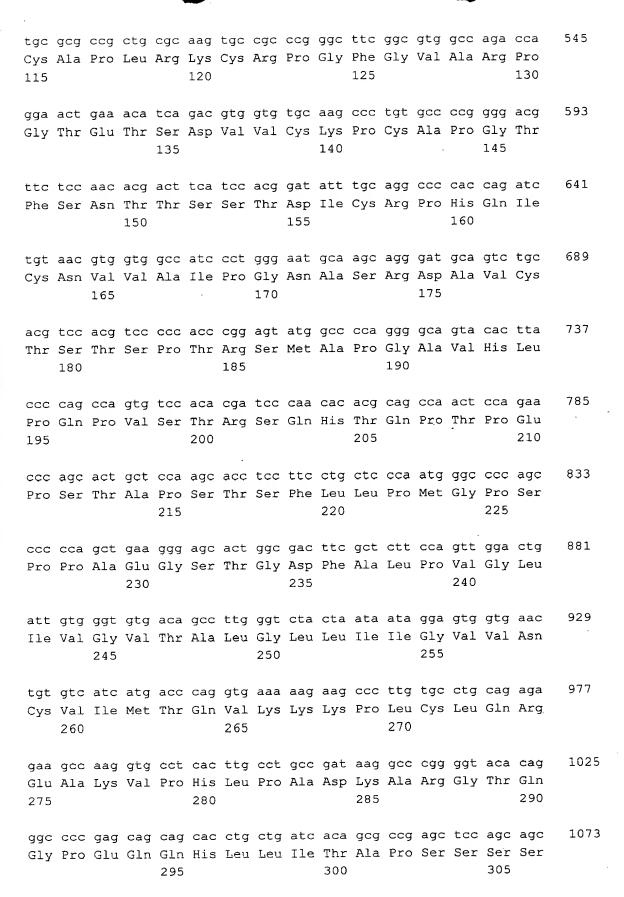


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| | cago | gggg | caa o | ccaa | accc | ca co | caca | accc | atq | gcg | ccc | gtc | gcc | gtc | tgg | gcc | 113 |
| | 3. | ,,,, | | | | _ | _ | | | Ala | | | | | | | |
| | | | | | | | | | | | -20 | | | | | -15 | |
| | | | | | | | | | | | 20 | | | | | 13 | |
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| | Ala | Leu | Ala | Val | Gly | Leu | Glu | Leu | Trp | Ala | Ala | Ala | His | Ala | Leu | Pro | |
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| | | | | | | | | | | | | | | | | | |
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| | Ala | Gln | Val | Ala | Phe | Thr | Pro | Tyr | Ala | Pro | Glu | Pro | Gly | Ser | Thr | Cys | • |
| | | | 5 | | | | | 10 | | | | | 15 | | | | |
| | | | | | | | | | | 4- | | - 4 | . | | | | 257 |
| | | ctc - | | | | | | | | | | | | | | | 257 |
| | Arg | Leu | Arg | Glu | Tyr | Tyr | | Gin | Thr | Ala | Gin | | Cys | Cys | ser | гÀг | |
| | | 20 | | | | | 25 | | | | | 30 | | | | | |
| | tac | tcg | ccg | ggc | caa | cat | gca | aaa | gtc | ttc | tgt | acc | aag | acc | tcg | gac | 305 |
| | _ | Ser | _ | | | | | | | | | | | | | | |
| | 35 | | | 1 | | 40 | | | | | 45 | | - | | | 50 | |
| | 5.0 | | | | | 10 | | | | | .0 | | | | | | |
| | acc | gtg | tgt | gac | tcc | tgt | gag | gac | agc | aca | tac | acc | cag | ctc | tgg | aac | 353 |
| | Thr | Val | Cys | Asp | Ser | Cys | Glu | Asp | Ser | Thr | Tyr | Thr | Gln | Leu | Trp | Asn | • |
| | | | | | 55 | | | | | 60 | | | | | 65 | | |
| | | | | | | | | | ~~~ | + ~ ~ | ~~~ | +~+ | 200 | + 0+ | ~~~ | ~~~ | 401 |
| | | gtt | | | | | | | | | | | | | | | 401 |
| | Trp | Val | Pro | | Cys | Leu | Ser | Cys | | ser | Arg | Cys | ser | | Asp | GIII | |
| | | | | 70 | | | | | 75 | | | | | 80 | | | |
| | ata | gaa | act | caa | qcc | tac | act | caa | gaa | cag | aac | cgc | atc | tgc | acc | tgc | 449 |
| | | Glu | | | | | | | | | | | | | | | |
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| | | | 55 | | | | | 20 | | | | | | | | | |
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| | | Pro | | | | | | | | | | | | | | | |
| | | 100 | | | | | 105 | | | | | 110 | | | | | |



| ı | | | | | | | | | | | | | | | | |
|-----|------|------------|------|------|------|------|------|-------|------|------|------|------|------|-------------------|--------|------|
| - | | | | | | | | | | | | | | ccc | | 1121 |
| | | | | | | | | | | | | | | ggg Gly | | 1169 |
| _ | | | | | | | | | | | | | | cat His | | 1217 |
| | | | | | | | | | | | | | | tct Ser | | 1265 |
| | _ | | | | | | | | | | | | | gac Asp 385 | | 1313 |
| _ | | _ | | | | | | | | | | | | ttc Phe | | 1361 |
| _ | | _ | | | | | | | | | | | | acc Thr | | 1409 |
| _ | - | | | | | | | | | | | | | gat Asp | | 1457 |
| | | aag Lys | | | | cca | ggcc | ggt (| gtgg | gctg | tg t | cgta | gcca | a | | 1505 |
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